

REMARKS

Applicants respectfully request entry of the above amendments to the claims and reconsideration of the application in light of the amendments to the claims and the arguments presented below.

The pending claims are set forth above. Claims 20-21 and 40-43 are currently pending. Claims 20, 40, 42-43 are currently amended. The amendments to the pending claims are made without prejudice or disclaimer, do not constitute amendments to overcome any prior art rejections under U.S.C. §§ 102 or 103, and are fully supported by the specification as filed. No new matter has been added as a result of the above amendments. The rejections set forth in the Office Action have been overcome by amendment or are traversed by argument below.

Applicants thank the Examiner for withdrawing rejections under 35 U.S.C. § 112, and under 35 U.S.C. § 102(b) in view of Cheng et al. and Daschner et al.

1. Objection to the Specification

Applicants have amended the specification at page 27, line 10 by deleting the embedded hyperlink. Applicants thank the Examiner for noticing the inconsistency.

2. Claim Rejections under 35 USC §112, second paragraph

Claims 20, 21 and 40-43 stand rejected under 35 USC §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Action asserts that the claims are vague and indefinite because it is not clear how the claimed invention can be achieved by the method steps recited in the claims. More specifically, the Action asserts that the method steps fail to achieve the purpose of the claim recited in the preamble because the preamble is directed towards a method of identifying taxane resistant tumor or tumor cells whereas the method steps are directed towards comparing gene expression between the tumor cells and the non-tumor cells. Applicants respectfully traverse.

Applicants respectfully direct the Examiner's attention to the final step of claim 20 (for example), wherein the relevant portions supporting their position are emphasized:

c) identifying the tumor or cells within the tumor to be resistant to taxane chemotherapeutic drugs when the gene expression levels of one or a plurality of said genes is increased in the tumor sample when compared to gene expression levels in the non-tumor sample

Applicants respectfully submit that the claims 20, 21 and 40-43 are directed towards identifying taxane resistant tumors or tumor cells in a tumor sample or cells. The emphasized portion fulfills the recitation in the preamble, that the methods are directed to identifying taxane-resistant tumors or tumor

cells using the claimed methods. Consequently, the method steps are directed towards comparing the expression of genes that have been identified in the specification, such as in Table III on page 30, as specifically having increased expression in taxane resistant tumors or tumor cells than the non-tumor cells. While it is possible to identify taxane-resistant tumors by treating the patient with taxane and determining that the treatment has failed, the pending claims are directed at methods for identifying taxane-resistant tumors without subjecting a patient having a resistant tumor to the effects of taxane. Thus, which the Action is correct that the method is directed towards identifying differential expression of certain genes in a tumor or cells within a tumor, the purpose of the method recited in the preamble is achieved by detecting said differential expression, due to the relationship between taxane resistance and differential gene expression disclosed in the specification. Support for the recited methods can be found in the specification, *inter alia*, on page 6. Thus, the method steps recited in claims 20, 21 and 40-43 fulfill the purpose of the preamble and are not indefinite.

Applicants therefore, request the Examiner to reconsider and withdraw this ground of rejection.

3. Claim Rejections under 35 USC §112, first paragraph

Claims 20, 21 and 40-43 stand rejected under 35 USC §112, first paragraph for failing to comply with the written description requirement. That Action asserts that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor(s) at the time the application was filed had possession of the claimed invention. More specifically, the Action asserts that the claims recite GenBank Accession Nos which are not supported by specification. The Action acknowledges that the specification as filed provides list of names of the genes with altered gene expression in chemotherapeutic drug resistant cells compared to the sensitive cells. The Action, however, argues that the specification does not provide sufficient support for the relationship of the names of the listed genes with the GenBank Accession Nos recited in the claims.

The Action further asserts that since the application does not provide structural identity as nucleotide or amino acid sequence, therefore one of skill in the art cannot determine from the disclosure alone whether the sequences claimed are identical to the sequences contained in the database under the accession no. at the time of filing. The Action also asserts that one could not determine based on accession nos alone which entry for a sequence is claimed if the sequence is modified or revised after the time of filing. Applicants respectfully traverse.

Applicants respectfully submit that the GenBank Accession Nos for all of the genes recited in the claims were available at a public database (as also acknowledged by the Office in the Action) and were, therefore, part of the general knowledge in the art at the time of filing of the application. It is black letter law that a specification “need not teach, and preferably omits, what is well known in the art.” *Spectra-*

Physics, Inc. v. Coherent, Inc., 827 F.2d 1524, 1534, 3 USPQ2d 1737, 1743 (Fed. Cir. 1987). Moreover, the quantum of evidence required and the standard that must be met is whether the skilled worker would know *which* genes were intended to be encompassed by Applicants' claims. The Action provides no evidence that the skilled worker would experience any confusion as to the identity of these genes.

To that end, Applicants submit Exhibit I showing gene sequence revision history that is available on the GenBank public database (<http://www.ncbi.nlm.nih.gov/entrez/sutils/girevhist.cgi>). As is evident from the Exhibit, the dates at which the sequences were first seen on the public database for all GenBank Accession Nos corresponding to the recited genes were before the filing date of the current application. Consequently, the relationship between the listed genes and the GenBank Accession Nos was part of the public knowledge and one of skill in the art.

Furthermore, each of the GenBank Accession Nos corresponded to only one sequence. Thus, one of skill in the art would have understood that the sequence recited in the claim (but, it is important to realize, not itself being claimed) is the sequence disclosed on the public database at the time of filing. Additionally, for the genes that have a second version of the gene sequence submitted after the filing of current application, the second version sequence is 100% identical to the first version of the sequence. Thus, one of skill in the art could easily determine which entry for a sequence was being claimed by the Applicants.

Applicants, therefore request the Examiner to overcome this ground of rejection.

4. Claim Rejections under 35 USC §102(b)

A) Claims 20, 21 and 40-44 stand rejected under 35 USC §102(b) as being anticipated by Mechetner et al. (Clin. Cancer Res., Vol. 4, pp. 389-98 (1998)) as evidenced by Sharom F et al. (J Bioenerg Biomembr, Vol 27, page 15-22, abstract) and Gottesman et al. (Nature Review, col 2, page 48-58, 2002). The Action asserts that Mechetner et al. discloses a method for identifying a tumor and cells that are resistant to taxol by increased expression of P-glycoprotein in human breast cancer cells. The action based its assertion on the teachings of Sharom et al and Gottesman et al. that P-glycoprotein has ATPase activity, and the disclosure of Mechetner that teaches methods for determination of expression of P-glycoprotein and teaches strong correlation between Pgp expression and degree of taxol resistance in clinical specimens.

Applicants have amended the claim 20 and 42 and the scope of the amended claims does not encompass ATPase. Furthermore, Applicants respectfully submit that claims 40 and 43 are directed towards determining expression levels of ATPase with one or more of the other genes recited in the pending claims 40 and 43. Therefore, claims 40 and 43 are directed towards determining expression levels of at least 2 or more genes, wherein one gene is ATPase. The cited reference, on the other hand, teaches measurement of ATPase alone. Hence, the reference does not teach each and every element of the recited claims 40 and 43, and therefore, can not

anticipate the claims.

Applicants therefore request the Examiner to reconsider and withdraw this ground of rejection.

B) Claims 20, 21, 40-44 stand rejected under 35 USC §102(b) as being anticipated by Junkun et al. (J. Cell. Biochem., Vol 53, pp. 135-44 (1993)) or U.S. Patent No. 5,679,350. Action asserts that Junkun et al. discloses a method of determining and comparing levels of expression of Urokinase receptor in tumor and non-tumor cells. Furthermore, Junkun et al. teaches the methods in breast cancer cells and discloses that malignant tumors express higher levels than normal breast tissues. Applicants respectfully traverse.

Applicants respectfully submit that the claims of the instant application require the identification of cells and/or tumors that are "resistant to taxane chemotherapeutic drugs." Jankun *et al.* and the '350 patent disclose methods directed toward the identification of cells having higher expression levels of Urokinase plasminogen activator receptor (uPAR), and teach that certain malignant cells show higher levels of uPAR expression. The instant claims are drawn to methods of identifying tumors and tumor cells that are resistant to taxane chemotherapeutic drugs. Neither Jankun *et al.* nor the '350 patent purports or suggests the identification of tumors and/or cells that are "resistant to taxane chemotherapeutic drugs." Consequently, since these references do not teach that levels of uPAR expression have anything to do with resistance to taxane chemotherapeutic drugs, the claims are not anticipated by these references. Furthermore, Applicants have amended claims to clarify the invention.

In view of the argument presented above and the amendment, the claims are not anticipated by the cited reference. Applicants therefore request the Examiner to reconsider and withdraw this ground of rejection.

CONCLUSION

The Applicant respectfully contends that all conditions of patentability are met in the pending claims as amended or as originally presented. Allowance of the claims is thereby respectfully solicited.

If there are any questions or comments regarding this Response or application, the Examiner is encouraged to contact the undersigned representative as indicated below at 312-913-0001.

Respectfully submitted,
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